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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| EXAMINER | |
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| CORDERO GARCIA, MARCELA M | |
| **ART UNIT** | **PAPER NUMBER** |
| 1654 | |

DATE MAILED: 11/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/728,082 | CRUZ, ANTONIO | |
| | Examiner | Art Unit | |
| | Marcela M. Cordero Garcia | 1654 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *10 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *37-41,48-50 and 54-62* is/are pending in the application.

4a) Of the above claim(s) *49,56,58,60 and 62* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *37-41, 48,50 and 54-55, 57, 59, 61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

Applicant's election of Group IV, drawn a method of treating a diabetes patient (claims 37-41, 48-50 and 54-62), and of the species consisting of human serum albumin conjugated to gastrin 17 (Leu15) as follows: "(human serum albumin)-Glp-Gly-Pro-Trp-Leu-Glu-Glu-Glu-Glu-Glu-Ala-Tyr-Gly-Trp-Leu-Asp-Phe-$NH_2$" (claims 37-41, 48-50 and 54-55, 57, 59, 61 readable thereon) in the reply filed on July 7, 2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 49, 56, 58, 60 and 62 are withdrawn as not drawn to the elected species.

Claims 37-41, 48, 50 and 54-55, 57, 59, 61 are presented for examination on the merits as they read upon Applicant's elected species.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 37-41, 48, 50 and 54-55, 57, 59, 61 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP 2163.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In Regents of the University of California v. Eli Lilly & Co., the court stated:

"A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by

structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials. Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606; In re Smythe, 480 F.2d 1376, 1383, 178 USPQ 279, 284-85 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus. . . ."). Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. The MPEP does state that for generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP 2163. Although the MPEP does not define what constitute a sufficient number of representative, the Courts have indicated what do not constitute a representative number species to adequately describe a broad generic. In Gostelli, the Court determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. In re Gostelli, 872 F.2d at 1012, 10 USPQ2d at 1618.

***In the instant case, the claims are drawn to a method of treating diabetes with a gastrin compound comprising Z-$Y_m$-$X_n$-$AA_1$-$AA_2$-$AA_3$-$AA_4$-$AA_5$-$AA_6$, wherein Z is a polymer, AA1 is Tyr of Phe, AA2 is Gly, Ala or Ser, AA3 is Trp, Val or Ile, AA4 is Met or Leu, AA5 is Asp or Glu, and AA6 is Phe or Tyr, Ym is an optional***

***spacer, and X is selected from any consecutive portions of residues 1-28 of SEQ ID No: 1, residues 1-28 of SEQ ID NO: 2, residues 1-11 of SEQ ID NO: 3, and residues 1-11 of SEQ ID NO: 4.*** The instant disclosure (e.g., page 2, lines 18-28) does not teach how to make and use this gastrin compounds in regards to the limitless structural variations with respect to using and incorporating any Z polymer in the therapeutic composition as encompassed by the instant claims, since Z encompasses any polymers, proteins and carbohydrates (page 3, lines 19-22), and with regards to the limitless optional embodiments of the spacer $Y_m$. In addition, the consecutive residue portions of residues 1-28 of SEQ IDs NOs:1-2 and residues 1-11 of SEQ ID NOs:3-4 encompass any possible combination from 2 consecutive amino acids, 3 consecutive, 4 consecutive, 5 consecutive, 6 consecutive, and so forth up to 28 or 11 consecutive amino acids respectively. The generic statements regarding the Z polymer, the optional spacer and the X group selected from any consecutive amino acid residues of SEQ ID Nos 1-4 do not provide ample written description for the compounds as to one would make such compounds to still retain anti-diabetic therapeutic activity. The specification does provide examples of what qualify as compounds of the claimed invention, however, these are limited to PEG and human serum albumin polymers with $(GA)_5$ as the optional linker or the optional linker absent and with $AA_1$-$AA_2$-$AA_3$-$AA_4$-$AA_5$-$AA_6$ corresponding to the known 6 residue gastrin terminal sequence and with X being consecutive portions 1-28, 2-28, 5-28 and 1-11, 2-11 and 5-11 of known SEQ ID Nos: 2 and 4 respectively, which correspond to the known gastrin 34 (big gastrin), gastrin 17 (little gastrin) and two N-terminal (i.e., not internal) truncations thereof.

As stated earlier, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable claim 1 is a broad generic with respect all possible compounds encompassed by the claims. The possible structural variations are limitless to any class of polymer without limitation and including broadly peptides as polymers and carbohydrates, and the optional spacer being any spacer without limitation. It must not be forgotten that the MPEP states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. Here, though the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the compounds beyond compounds disclosed in the examples in the specification. Moreover, the specification lack sufficient variety of species to reflect this variance in the genus since the specification does not provide any examples of derivatives. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, it is deemed that the specification fails to provide

adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 37-41, 48, 50 and 54-55, 57, 59, 61 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 37 is rendered vague and indefinite because at line 2, the coefficient n in -$X_n$- is not defined therein.

Claim 38 is rendered vague and indefinite because the limitation "less than the frequency of administration of a native gastrin". With regards to this limitation, it is unclear whether this is referred to a method wherein both a native and a modified gastrin are being administered during the treatment or if it refers to a standard frequency of administration to which the instant invention needs to be compared to.

For the art rejection below, please note that the sequence of gastrin 17 (Leu) has the following sequence: pGlu-Gly-Pro-Trp-Leu-Glu-Glu-Glu-Glu-Glu-Ala-Tyr-Gly-Trp-Leu-Asp-Phe-$NH_2$ as evidenced by Sigma Aldrich catalog [http://www.sigmaaldrich.com/catalog/search/ProductDetail?ProdNo=G9145&Brand=SIGMA, accessed online 11/1/06].

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 37-41, 48, 50 and 54-55, 57, 59, 61 are rejected under 35 U.S.C. 102(b) as being anticipated by Brand (US 6,992,060) in view of Bridon et al (US 6,329,336).

Brand teaches a method of treating a subject having diabetes, comprising administering gastrin 17 (Leu15): pGlu-Gly-Pro-Trp-Leu-Glu-Glu-Glu-Glu-Glu-Ala-Tyr-Gly-Trp-Leu-Asp-Phe-$NH_2$ comprising: $Y_m$-$X_n$-$AA_1$-$AA_2$-$AA_3$-$AA_4$-$AA_5$-$AA_6$, wherein $AA_1$ is Tyr, $AA_2$ is Gly, $AA_3$ is Trp, $AA_4$ is Leu, $AA_5$ is Asp, $AA_6$ is Phe, the $AA_6$ being amidated; Xn is the consecutive portion of residues 1-11 of SEQ ID NO:3: pGlu-Gly-Pro-Trp- Leu-Glu-Glu-Glu-Glu- Glu-Ala (see instant disclosure, page 3, lines 19-22), $Y_m$ is not present; [see, e.g., column 7, lines 15-35, Example 2, claims 1-2]. Brand teaches measuring a physiological indicator of islet neogenesis (e.g., column 9, lines 23-30, column 10, lines 38-61, Figs 1-5, 7), measuring fasting blood glucose (e.g., Figs. 6 and 8) decreasing insulin dependency (e.g., Fig. 7) and stimulating the expression of the hormone insulin (e.g., Example 2).

Brand does not teach conjugating gastrin 17 (Leu15) to human serum albumin.

Bridon et al. teaches treating diabetes conjugating to serum albumin insulinotropic peptides (peptides that stimulate or cause the stimulation of, the synthesis or expression of the hormone insulin) to improve its bio-availability and extend its half-life while maintaining low toxicity and therapeutic advantage (column 4, lines 55-63) and using a wide selection of protective groups and linkers to select the binding site of the albumin, e.g., to attach to the N-terminal end of the peptide (e.g., columns 12-18 and Examples).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Brand by conjugating the insulinotropic peptide gastrin 17(Leu) to albumin as taught by Bridon et al (e.g., column 1, lines 42-67 and column 2, lines 35-39, claims 1, 11-14). The skilled artisan would have been motivated to do so because conjugating it to albumin would improve its bio-availability, and extend its half-life, while maintaining low toxicity and therapeutic advantage (Bridon et al., column 4, lines 55-63). There would have been a reasonable expectation of success, given that this conjugation is effective for a broad group of insulinotropic peptides of similar size than gastrin 17 (Leu15) as taught by Bridon et al. (e.g. Examples and Sequence Listing) and because Bridon et al. teaches that the selection of protective groups and linkers allows one of skill in the art to select the binding site of such albumin, e.g., to attach to the N-terminal end of the peptide (columns 12-18, Examples). Thus the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 37-41, 48, 50 and 54-55, 57, 59, 61 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, 7-10, 12-14, 24-26, 33-45, 101-107 and 110 of copending Application No. 10/691,123. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instantly claimed invention and the invention claimed in Application '123 are both drawn to a method of treating diabetes comprising administering a gastrin/CCK receptor ligand of the formula $Z\text{-}Y_m\text{-}X_n\text{-}AA_1\text{-}AA_2\text{-}AA_3\text{-}AA_4\text{-}AA_5\text{-}AA_6$. Further, the instantly claimed method encompasses and/or is encompassed by the claimed method of Application '123. For example, gastrin 17 reads upon the instantly claimed compound with Z is residues 1-9 of SEQ ID NO: 4, $Y_m$ is not present,

$X_n$ is residues 10-11 of SEQ ID NO: 4, wherein $AA_1$ is Tyr, $AA_2$ is Gly, $AA_3$ is Trp, $AA_4$ is Leu, $AA_5$ is Asp, $AA_6$ is Phe, the $AA_6$ being amidated. Similarly, gastrin 34 reads upon the instantly claimed inventions in both applications.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 37-41, 48, 50 and 54-55, 57, 59, 61 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-15, 21-45, 72-91 and 101-110 of copending Application No. 10/532,395. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instantly claimed invention and the invention claimed in Application '395 are both drawn to a method of treating diabetes comprising administering a gastrin/CCK receptor ligand of the formula $Z\text{-}Y_m\text{-}X_n\text{-}AA_1\text{-}AA_2\text{-}AA_3\text{-}AA_4\text{-}AA_5\text{-}AA_6$. Further, the instantly claimed method encompasses and/or is encompassed by the claimed method of Application '395. For example, gastrin 17 reads upon the instantly claimed compound with Z is residues 1-9 of SEQ ID NO: 4, $Y_m$ is not present, $X_n$ is residues 10-11 of SEQ ID NO: 4, wherein $AA_1$ is Tyr, $AA_2$ is Gly, $AA_3$ is Trp, $AA_4$ is Leu, $AA_5$ is Asp, $AA_6$ is Phe, the $AA_6$ being amidated. Similarly, gastrin 34 reads upon the instantly claimed inventions in both applications.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

***Conclusion***

No claim is allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marcela M. Cordero Garcia whose telephone number is (571) 272-2939. The examiner can normally be reached on M-Th 7:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia J. Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Marcela M Cordero Garcia

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MMCG 10/06

11/17/06
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PRIMARY EXAMINER